REMARKS

The claims have been amended to correct them and make the terms consistent, without abbreviations. It is submitted, therefore, that the objections to the claims should be withdrawn.

In response to the rejection under 35 USC §112, paragraph 1 enclosed is a Declaration of Peter Lennartz, Ph.D., indicating that there is no criticality to the amount of compressive force used to create the compactate that results from compression. The Lennartz Declaration also states that examples 3 and 4, according to the claimed invention, were compacted from a composition having the particle size claimed. It was found, however, that the claimed particle size and claimed in-vitro release profiles were important to achieve the claimed, sustained plasma levels of the active MHD (monohydroxydihydrocarbamazepine).

It is asserted in the first office action that the predictability in the art is low as to what combination of ingredients and dosage formulations will result in the claimed release profile and plasma concentrations. This is incorrect insofar as the excipients and films that may be used to prepare the claimed oxcarbazepine compactates.

As stated in the parent application referred to in the office action, there are various ways to provide a sustained-release composition. One way of providing a sustained-release composition is coating the tablets with a film customary for sustained-release. Such embodiment is, e.g., described in WO 2004/026 314 (claiming a later priority). Plastics suitable for the construction of the film for sustained-release are known to those skilled in the art. Another way of providing a sustained-release composition can be achieved with a compacting technique. An optional film-forming technique is described, e.g., in method claims 13, 15 and 16. This optional film can be applied in addition to compacting. It is known to those skilled in the art that the release time can be controlled within a range by variation of the composition of the film and/or by variation of the layer thickness of the film, and/or, as exemplified, by a compaction method.

It is important to note that the present invention is based on the finding that typical sustained-release formulations with subsequently low in-vitro release profiles have proved ineffective (see description). The person skilled in the art is taught to formulate a sustained-release composition, where the in-vitro release pattern of oxcarbazepine is only slightly below that of tablets commonly marketed. Such commonly marketed tablets are,

e.g., sold under the trade name Trileptal®. The Tileptal® tablets and similar tablets release oxcarbazepine in a very fast manner (see comparison example and Figs. 6 and 7 of the present application), and are unsuitable for once-a-day administration.

The present application teaches to adjust the in-vitro release in accordance with the requirements of claim 1 with methods well-known in the art in order to obtain a pharmaceutical preparation which is suitable for once-a-day administration. In other words, the present application, for the first time, provides the person skilled in the art with an "in-vivo-in-vitro correlation". Once a person skilled in the art is taught to which values the in-vitro release profile is to be adjusted in order to obtain an in vivo release profile suitable for once-a-day administration, then the necessary adjustments can easily be made using methods well-known in the art.

Furthermore, the present application teaches that the release profile can be achieved using the particular particle size described in the examples. The oxcarbazepine particles of the examples according to the invention had a particle size within the claimed range, whereas the oxcarbazepine particle size of the Tileptal® tablets is much smaller. Thus, there is no lack of predictability but, to the contrary, the subject-matter of the claims is non-obvious over the prior art because surprisingly, an inventive release profile, suitable for once daily administration, is achieved using oxcarbazepine of the claimed particle size distribution. Further, the compacting method is described in example 1 of the present application and is not critical to achieving the release profiles, as set forth in the enclosed Declaration of Peter Lennartz.

The commonly marketed oxcarbazepine tablets sold under the trade name Trileptal® release oxcarbazepine in a very fast manner (unsuitable for once-a-day administration) although the in-vitro release profile of Trileptal® is not much different than the in-vitro release profile disclosed and claimed in the present application. The substantial variation of in-vivo vs. in-vitro release profiles, however, cannot be ignored, as pointed out with reference to the comparative examples of applicants' specification.

THE TRILEPTAL® FORMULATION IS PUBLISHED

The composition of Lang et al. (WO 01/32183) does not provide an essentially constant level of active MHD over a 24 hour period, as taught herein by applicants.

The Lang et al. '183 publication (Trileptal®) does not provide the in-vitro or in-vivo release profiles claimed herein by applicants.

The formulation of Trileptal® has been published by Novartis Pharma, see e.g. the attached summary (Exhibit A) of product characteristics ("Fachinformation") of November 2005, Section 6. entitled "Pharmazeutische Angaben" (pharmaceutical information), 6.1 "Sonstige Bestandteile" (other ingredients). From this document it can be gathered that the film tablets contain a core ("Kern") comprising highly dispersed silica ("Hochdisperses Siliziumdioxid"), microcrystalline cellulose ("Mikrokristalline Celluslose"), hypromellose ("Hypromellose"), which in fact is Cellulose HPM 603, Crosspovidone ("Crosspovidon"), and magnesium stearate ("Magnesiumstearat"). The film comprises hypromellose ("Hypromellose"), talc ("Talkum"), titanium dioxide ("Titandioxid"), and further (see e.g. 300 mg Trileptal® tablets) iron(II) oxide yellow, which corresponds to ironoxihydrate E 172 ("Eisenoxyhydrat E 172") and a polyethylene glycol ("Macocol 8000"). Thus, the composition of Trileptal® corresponds exactly to the composition disclosed in Lang et al. WO 01/32183, Example I. For the sake of simplicity we provide a comparison of the ingredients of Lang et al. WO 01/32183, Example 1 with the attached summary of product characteristics for Trileptal®:

Example 1 **Lang et al. - WO 01/32183**	**Trileptal, Novartis Pharma** **Fachinformation/SPC (Summary of Product Characteristics)** **Registration No. 47357.01.00**	**Comparison**
Tablet core	Kern (Tablet core)	Tablet core
Tripletal AS extra fine	Oxcarbazepin (Oxcarbazepine)	Active Pharmaceutical ingredient - identical
Cellulose HPM 603	Hypromellose (e.g., Cellulose HPM 603)	Binder, polymer - identical
Microcrystalline Cellulose	Mikrokristalline Cellulose (Microcrystalline Cellulose)	Binder, filler - identical
Colloidal anhydrous silicia	Hochdisperses Siliziumdioxid (Collodial anhydrous silicia)	Flow conditioner - identical
Magnesium stearate	Magnesiumstearat (Magnesium stearate)	Lubricant - identical
Crosspovidone	Crosspovidon (Crosspovidone)	Disintegrant - identical
Coating	Film (Coating)	Coating
Cellulose HPM 603	Hypromellose (e.g., Cellulose HPM 603)	Film former - identical
Iron (II) oxide (yellow) 17268	Eisenoxidhydrat (e 172) (Iron (ii) oxid)	Pigment - identical
Polyethylen glycol (PEG) 8000	Macrocol 8000 (Polyethylen glycol (PEG) 8000)	Plasticizer - identical

Talcum	Talkum (Talcum)	Antiadherent - identical
Titanium dioxide	Titandioxid (E171) (Titanium dioxide)	Pigment - identical

Table: comparison of qualitative composition of Lang et al. and Trileptal®.

From this comparison it is evident that the composition of the tablets of oxcarbazepine of Example 1 of Lang et al. is identical to the Trileptal® tablets. Accordingly, applicant's comparative data truly represent the composition of Lang et al. Further, the particle size of the oxcarbazepine of Lang et al. is much smaller than that claimed by applicants herein (see Lang et al. page 7, lines 1-11).

Furthermore, it is stated at page 4, last paragraph to page 5, fourth paragraph of Lang et al. that the oral dosage forms according to said document display in vitro dissolution rates of not less than 70%, preferably not less than 90% dissolved after 30 minutes and not less than 80% dissolved after 60 minutes, as measured according to the USP-Paddle method (USP 24, Method 724, App. 2, in 1 L 1% sodium dodecyl sulphate solution as release medium, and at a stirring speed of 60 rpm). Applicant's measured the release profile of a 600 mg Trileptal® tablet in accordance with the method specified in Lang et al. The results are depicted in the following graph:

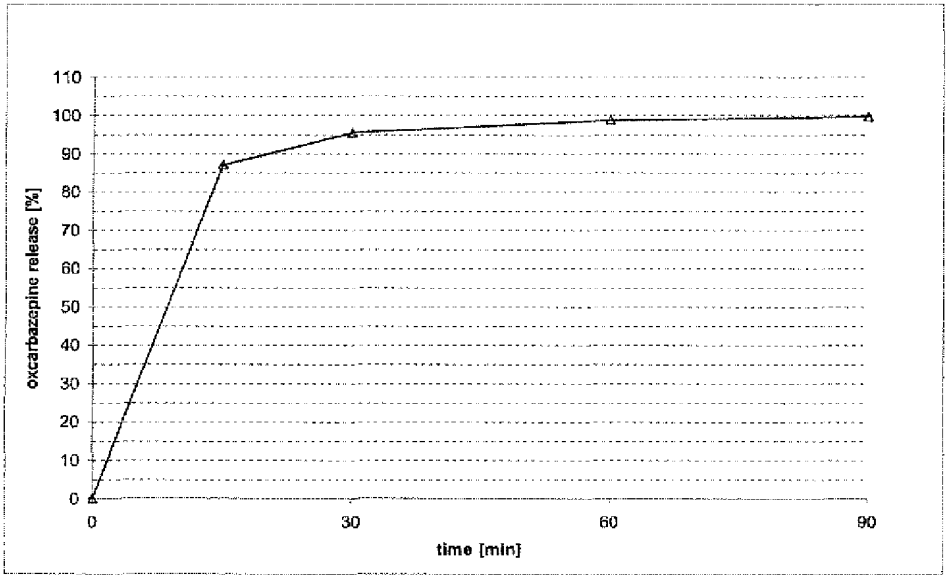

Figure: In-vitro release profile of 600 mg Trileptal® (USP 24, Method 724, App. 2, in 1 L 1% sodium dodecyl sulphate solution as release medium, and at a stirring speed of 60 rpm).

From the above graph it can be gathered that about 95% oxcarbazepine are released after 30 min, which is above 90% as required by Lang et al, page 5, 3rd paragraph.

This corroborates the above finding that the Trileptal® tablet is exemplary for the composition of Lang et al., Example 1.

The same Trileptal® tablet has been examined in the application as filed, and exhibits an in-vitro release profile, as measured under the conditions specified in claims 1 and 2 (USP 24, Method 724, App. 2, in 1 L 2% sodium dodecyl sulphate solution as release medium, and at a stirring speed of 75 rpm), outside the range as claimed in claim 2, see Fig. 3 of the present application:

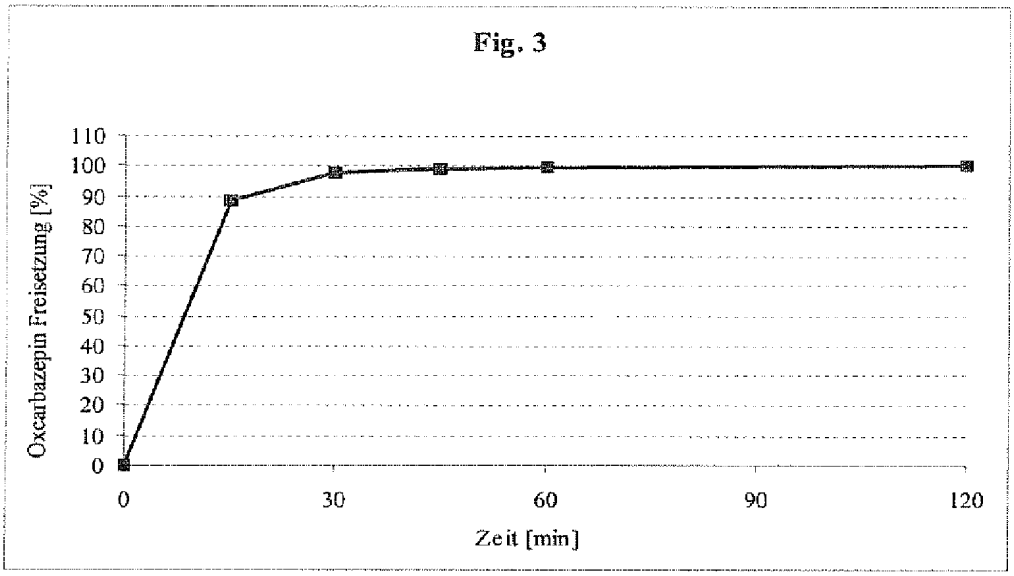

Figure: In-vitro release profile of 600 mg Trileptal® (USP 24, Method 724, App. 2, in 1 L 2% sodium dodecyl sulphate solution as release medium, and at a stirring speed of 75 rpm)

The release at 15 min. and at 30 min. is above the claimed range.

As shown in Fig. 4 of the present application, such tablet shows a fast in-vivo release of oxcarbazepine and its metabolite MHD, thereby rendering it unsuitable for effective once daily administration:

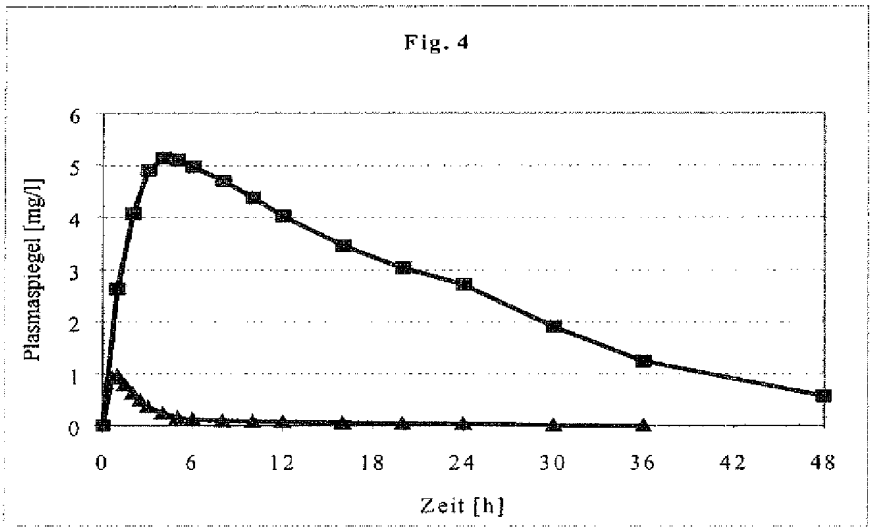

Figure: In-vivo release profile of 600 mg Trileptal® (oxcarbazepine and MHD levels).

In contrast, a composition having an in-vitro release profile, as measured under the conditions specified in applicants' claims (USP 24, Method 724, App. 2, in 1 L 2% sodium dodecyl sulphate solution as release medium, and at a stirring speed of 75 rpm) , inside the range as claimed in claim 1, see Fig. 4 of the present application, exhibits an extended in-vivo release of both oxcarbazepine and its metabolite MHD, see Fig. 5 of the present application:

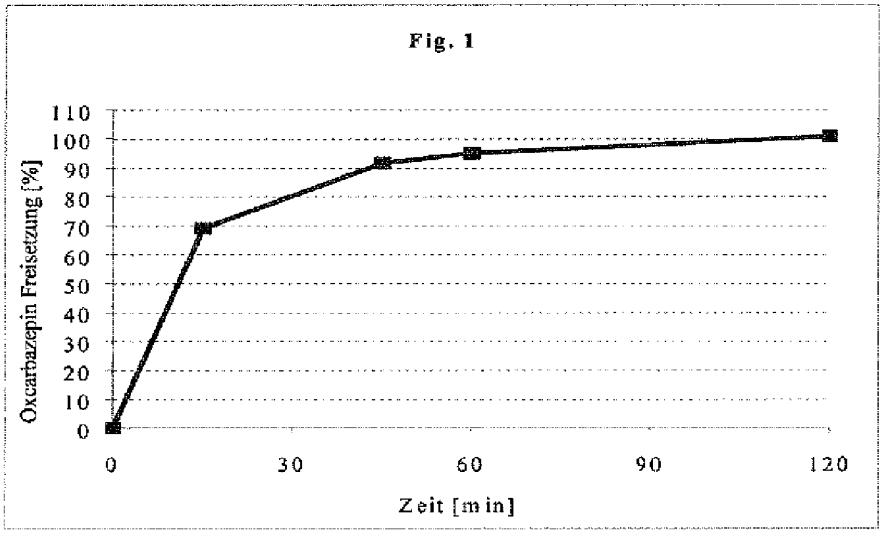

Figure: In-vitro release profile of 600 mg oxcarbazepine formulation according to Example 1 of the present application (USP 24, Method 724, App. 2, in 1 L 2% sodium dodecyl sulphate solution as release medium, and at a stirring speed of 75 rpm)

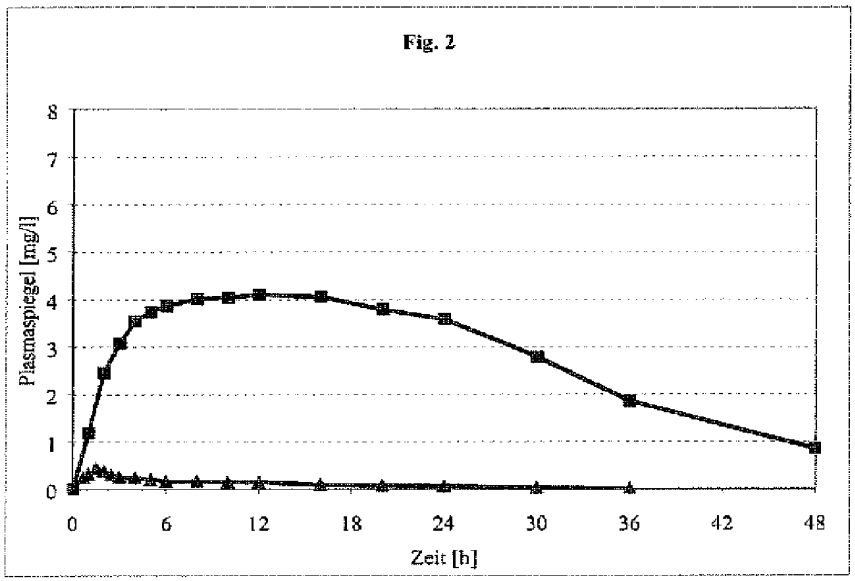

Figure: In-vivo release profile of 600 mg oxcarbazepine formulation according to Example 1 of the present application.

The in-vitro release profile of the composition according to Fig. 6 has been examined under conditions specified in Lang et a1., page 4, 4th paragraph (USP 24, Method 724, App. 2, in 1 L 1% sodium dodecyl sulphate solution as release medium, and at a stirring speed of 60 rpm). The release profile is depicted in the following graph:

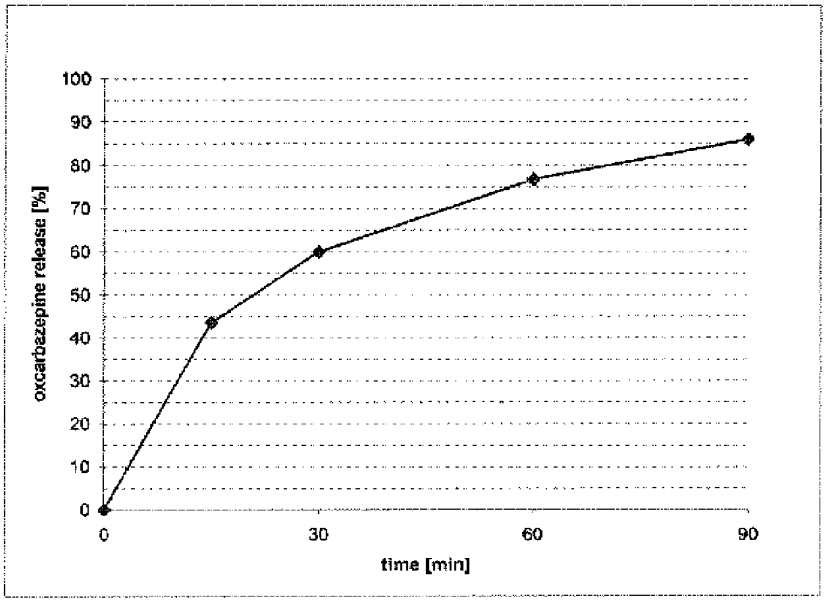

Figure: In-vitro release profile of 600 mg oxcarbazepine formulation according to Example 1 of the present application measured in accordance with Lang et al. method (USP 24, Method 724, App. 2, in 1 L 1% sodium dodecyl sulphate solution as release medium, and at a stirring speed of 60 rpm).

This graph shows that a composition according to the invention has an in-vitro release at 30 min. below 70% (i.e. about 60%), and at 80 min. below 80%, and therefore does not comply with the requirements specified at page 4, last paragraph of Lang et al.

To summarize the above, applicant's have conclusively shown that a composition as disclosed in Example 1 of Lang et al. does not meet the requirements of claim 1 of the present application, and is in fact representative for compositions having a fast in-vivo release profile.

Such compositions have the disadvantages discussed in the introductory part of the present application.

All claims are of proper form and scope for allowance. Early and favorable consideration is respectfully requested.

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Respectfully submitted,

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